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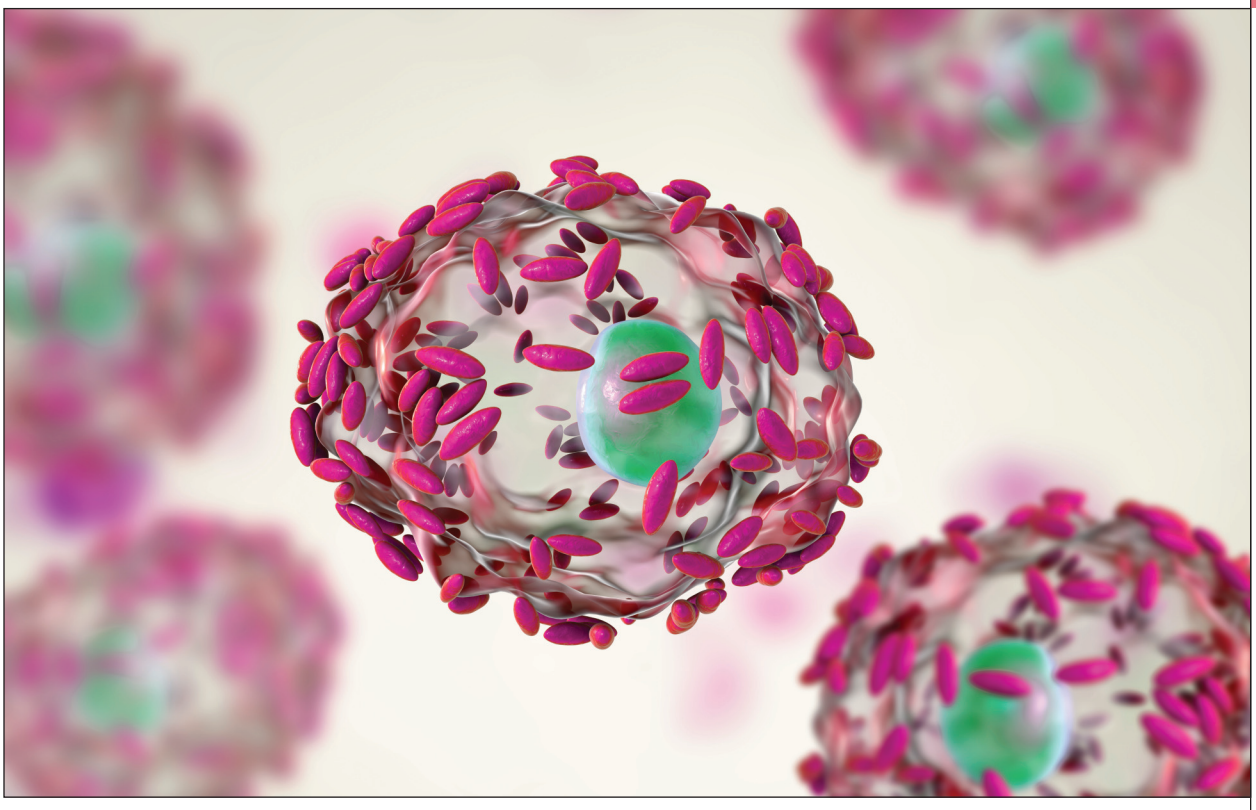


Dr_Microbe

Recurrent bacterial vaginosis

Abstract: Bacterial vaginosis recurrence is common but can lead to frequent bothersome symptoms associated with infection. This article reviews evidence-based options for practicing providers to improve patient outcomes. Bacterial vaginosis increases the risk of acquiring sexually transmitted infections, including HIV. Adequate treatment is essential to help avoid adverse patient outcomes.

By Kelly Ellington, DNP, APRN, WHNP-BC, RNC-OB and Scott J. Saccomano, PhD, RN, GNP-BC

According to the CDC, bacterial vaginosis (BV) is one of the most common vaginal disorders in women ages 14-49.[1] Estimated BV occurrence in women of reproductive age is about 29%.[1-3] In the US alone, BV affects more than 21 million women.[1,3] BV is more common in non-White women, affecting approximately 50% of Black Americans and 32% of Mexican Americans. Globally it is found most commonly in parts of Africa and least commonly in Asia and Europe.[2] Complications from BV include increased risk of sexually transmitted diseases including HIV, pelvic inflammatory disease, preterm labor, and postoperative infections.[3,4]

Risk factors

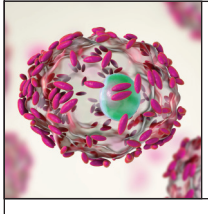
The vaginal pH is normally controlled by *Lactobacilli*, native bacterial flora that keeps the vagina slightly acidic to counteract overgrowth of pathogenic bacteria. When the natural balance of bacterial flora in the vagina is upset, the patient is at risk for BV. Certain factors can increase a woman's risk for BV:

Keywords: bacterial vaginosis, HIV, preterm delivery, recurrent bacterial vaginosis, STIs

- Smoking: Tobacco is thought to alter the physiology and structure of the flora of the vagina, increasing bacterial virulence. Nicotine metabolites have been found in the cervical mucous of female smokers. Smoking promotes an antiestrogen environment and elevates vaginal amines, which predisposes women to BV.[5,6]
- Douching: The use of commercial douching products alters the normal vaginal flora and vaginal pH, which are designed to protect the vagina from pathogens, and generates an environment that is more susceptible to pathogen overgrowth, increasing the risk of BV.[7,8]
- Multiple sexual partners: Although not a sexually transmitted disease, BV is promoted by certain sexual behaviors. New sexual partners and unprotected sex, both of which can present unfamiliar bacteria or microorganisms, contribute to increased BV risk.[9-11] Prevalence of BV in women who have sex with women may be as high as 50%.
- Intrauterine devices (IUDs): IUDs, which are effective pregnancy prevention devices, are associated with an increased risk of BV. Women with imbalance in their normal vaginal flora and who present with irregular bleeding while using IUDs are most at risk.[12]

Pathophysiology

The pathophysiology of BV is characterized by a modification in the vaginal bacterial flora and is poorly understood. Under normal circumstances, *Lactobacilli* are found in high concentrations in the vagina. *Lactobacilli* inhibit growth of pathogenic organisms by production of hydrogen peroxide and maintenance of vaginal pH in the normal range of 3.8 to 4.2 through lactic acid production.[13] The antimicrobial properties of lactic acid also inhibit the growth of pathogens. However, in BV, there is a shift in vaginal flora, with a reduction in the dominant *Lactobacillus* species and an overgrowth of anaerobic pathogens such as *Gardnerella vaginalis*, *Mobiluncus* species, and *Mycoplasma hominis*, and a subsequent elevation in pH. Anaerobic overgrowth is accompanied by an alteration of vaginal peptides into amines which become foul-smelling in high pH environments. Amines are implicated in the process of increased vaginal transudation (lubrication) and exfoliation of squamous cells producing the foul-smelling discharge associated with BV. The elevated vaginal pH sets the stage for *G. vaginalis* to adhere to the exfoliating epithelial cells, resulting in the development of characteristic clue cells, which are vaginal epithelial cells with adherent coccobacilli. Amines also provide a substrate for *M. hominis* growth. There is no one specific organism that is the cause of BV; it is caused by a group of pathogenic anaerobic organisms.[3,4,10-14]



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Clinical manifestations

Studies have estimated that 50% to 75% of women with BV are asymptomatic. Symptomatic women present with vaginal discharge and/or vaginal odor.[15] The discharge is off-white, thin, grayish, and smooth. BV has a characteristic disagreeable "fishy smell." The vaginal odor is frequently stronger after sexual intercourse and during menstruation.[15,16] BV alone normally does not cause other symptoms such as dysuria or vaginal itching.

NPs need to be aware of the consequences of BV, which has been associated with postpartum fever, posthysterectomy vaginal cuff cellulitis, postabortal infection, and endometrial infection. BV increases the risk of contracting sexually transmitted infections including HIV, herpes simplex virus type 2 (HSV-2), gonorrhea, chlamydia, and trichomonas infection.[15,17,18]

BV is a risk factor for increased incidence of preterm birth in pregnant women, and providers should be aware of associated risks especially with high-risk groups such as women with a history of preterm delivery. Premature rupture of membranes, preterm labor, intra-amniotic infection, and postpartum endometritis have been associated with symptomatic BV in some observational studies.[16] However, according to the CDC, there is insufficient evidence to recommend routine screening of asymptomatic pregnant women for BV.[16-18]

Diagnostic studies and differential diagnoses

The diagnosis of BV is easily accomplished in an outpatient office setting based upon Amsel criteria, which requires microscopy and is not complicated to perform.[19] Clinics without microscopes are unable to

perform the Amsel criteria method. The Amsel criteria requires vaginal discharge sampling with speculum examination. Three out of four criteria must be present to make an accurate diagnosis (see *Amsel diagnostic criteria*). NPs should be cautious about making the diagnosis based on patient-reported symptoms, such as a "fishy odor," which may guide differential diagnosis but does not establish a definitive diagnosis.[2] The "whiff test" is considered positive if the application of potassium hydroxide solution to the vaginal sample on a wet mount renders a fishy odor. Patient self-report of fishy-smelling discharge does not signify a positive whiff test. NPs utilizing Amsel criteria must be competent in the use of a microscope to identify clue cells.

Gram stain of vaginal discharge, otherwise known as the Spiegel criteria, is the gold standard for diagnosis of BV.[17,19] While the Spiegel criteria is utilized by researchers, it is not practical for NPs in outpatient office settings.

Newer technology diagnostics include a sialidase activity test, a DNA-probe, and polymerase chain reaction (PCR)-based assay vaginal swabs. The OSOM BVBlue system is a point-of-care chromogenic diagnostic test evaluating for sialidase enzyme activity in vaginal samples. It has good sensitivity and specificity and results can be read within 10 minutes.[20] The Affirm VPIII is a DNA diagnostic tool for detecting the presence of *G. vaginalis* at high levels.[18,20] This is a viable option for clinics without microscopy and the results of the test take about an hour. The enhanced technology provides more diagnostic options, but it comes with higher cost.[21] The newer tests are often not covered by insurance plans, which correlates with increased patient out-of-pocket expense.

The Papanicolaou smear is not reliable for BV diagnosis.[16] Vaginal cultures are not utilized in the diagnosis of BV.[16,17]

BV is often the diagnosis and frequently suspected with high vaginal pH (>4.5). Other possible causes of increased pH include trichomoniasis, atrophic vaginitis, and desquamative inflammatory vaginitis. The differential diagnoses can easily be limited by microscopic findings. Other differential possibilities can be eliminated with diagnostic studies and thorough history and physical exam findings.[15,17,18] Women with atrophic vaginitis, trichomoniasis, and desquamative inflammatory vaginitis often have signs and symptoms of vaginal inflammation and dyspareunia. Women with BV do not commonly have inflammatory signs and symptoms. Parabasal cells are often increased with atrophic vaginitis or desquamative inflammatory vaginitis and easily identified on a wet mount. Differential diagnosis should consider the possibility of a mixed infection with BV and a second microorganism such as *Candida* species or *Trichomonas vaginalis*.

Amsel diagnostic criteria[1-6]

Thin, grayish-white, smooth vaginal discharge
Positive whiff test (a fishy odor is produced when potassium hydroxide [KOH] is added to vaginal discharge sample)
Clue cells present on microscopy, at least 20% on wet mount
Vaginal pH > 4.5

Note: Three out of four criteria must be met; establishes accurate diagnosis of bacterial vaginosis in 90% of affected women.

Recurrent BV is defined as a confirmed diagnosis of BV three or more times within the same year.[22]

Disease management

A diagnosis of BV should be treated with a regimen outlined in the CDC guideline (see *CDC treatment guidelines for BV*).[16] Of note, providers should advise patients to avoid sexual activity or to use condoms during BV treatment.[16]

Secnidazole (Solosec), a single-dose oral granule antimicrobial, is the newest option for treatment of BV.[23] Unlike some of the other treatment options, the FDA has placed no warning regarding avoidance of alcohol consumption for secnidazole.

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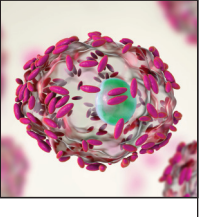
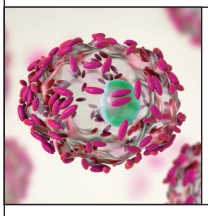


Treatment of recurrent BV. Data results from limited studies on treatment for recurrent BV are not definitive, but literature reveals some options which are off-label but commonly utilized in clinical practice. A treatment regimen focused on decreasing the chance of recurrence is 0.75% metronidazole vaginal gel twice

weekly for 4 to 6 months after completion of the initial CDC regimen.[22]

Treatment options for recurrent BV focused on eradication of pathogenic bacteria and/or to restore the natural vaginal microbiome have conflicting data regarding efficacy and are off-label.[24] Interventions include boric acid vaginal suppositories for 21 days followed by 0.75% metronidazole gel twice weekly for 4 to 6 months.[8,9] Caution must be exercised as boric acid can cause death if ingested orally; patients should be instructed to store it in a secure place out of reach of children. Hormonal contraception may have beneficial effects on vaginal epithelial cells.[22] BV-related microbes have been found in the male genitalia, however, studies evaluating concurrent treatment of male sexual partners of women with BV have failed to demonstrate benefit so this is not recommended.[25]



Women with BV report feeling self-conscious and uncomfortable and often avoid sexual encounters due to worries related to their symptoms.

Treatment of BV in pregnancy. Treatment is recommended for all symptomatic pregnant women. Symptomatic pregnant women can be treated with the recommended oral or vaginal regimens for nonpregnant women.[16,26] However, tinidazole should be avoided in pregnancy as limited data in animal studies suggest moderate risk. Asymptomatic pregnant women are not routinely screened or treated for BV.

CDC treatment guidelines for BV[16]

Recommended regimens	
Metronidazole *or*	500 mg orally twice daily for 7 days
Metronidazole gel 0.75% *or*	One full applicator (5 g) intravaginally once a day for 5 days
Clindamycin cream 2%* *or*	One full applicator (5 g) intravaginally at bedtime for 7 days
Alternative regimens	
Tinidazole *or*	2 g orally once daily for 2 days
Tinidazole *or*	1 g orally once daily for 5 days
Clindamycin *or*	300 mg orally twice daily for 7 days
Clindamycin vaginal suppository**	100 mg intravaginally once at bedtime for 3 days

Notes: Alcohol consumption should be avoided during treatment with metronidazole and tinidazole, including for 24 hours after the last dose of metronidazole and 72 hours after the last dose of tinidazole.

**Clindamycin cream is oil-based and may weaken latex or rubber condoms and diaphragms for 5 days after use. Refer to clindamycin product labeling for additional information.*

***Clindamycin vaginal suppositories use an oleaginous base that might weaken latex or rubber condoms and vaginal contraceptive diaphragms; use of such products within 72 hours following treatment is not recommended.*

Patient education

Multiple studies have associated sexual activity as a risk factor for BV.[27] Researchers lack the data to conclusively determine whether BV is sexually transmitted. There is an increased incidence of BV in people who have multiple sexual partners, women who have sex with women, and those who have unprotected sexual intercourse.[28] Alteration of at-risk behaviors such as limiting sexual partners, using condoms, and improved hygiene with sharing of sex toys can help protect against BV recurrence. Avoidance of douching is recommended to help prevent recurrent BV.

Use of estrogen-containing contraception may be protective.[29] The use of combined oral contraception is linked to increased vaginal colonization with *Lactobacilli* and reduced BV-associated microbiota. Patients with vaginal symptoms such as discharge or odor should seek prompt evaluation and treatment with evidence-based options. The effectiveness of probiotics in the prevention of BV is not yet clear.

Implications for practice

Untreated BV can increase the risk of acquiring sexually transmitted infections including HIV and may lead to pregnancy complications.[30] The CDC recommends testing all women with BV for HIV and other sexually transmitted infections.[16] BV increases risk of subsequent chlamydial or gonorrheal infection by almost two-fold.[27] BV is linked to an increase in HIV shedding, and HIV-infected women diagnosed with BV are more likely to transmit HIV to their sexual partners.[31] BV is a risk factor for HSV-2 infection. BV is correlated to increased risk of human papillomavirus (HPV) and is associated with HPV persistence.[30,31] Clinical consideration for asymptomatic BV in women with HPV coinfection may be warranted.

BV has been associated with a twofold increased risk of preterm delivery.[32] Spontaneous abortion rates in the first trimester are three- to fivefold higher in women with BV.[33] All pregnant individuals with symptomatic BV should be treated to relieve symptoms. Oral treatment is effective and has not been associated with adverse fetal or obstetric effects.[34] A systematic review including general obstetric populations found that treatment of asymptomatic infection does not reduce the incidence of preterm birth; therefore, routine screening is not currently recommended in pregnancy.[33,34]

Probiotics (live microorganisms used for health benefit) have been utilized alone or as an adjunct to antibiotic treatment of BV, however, a systematic review of probiotics for treatment of BV failed to find convincing evidence for or against efficacy.[35]

BV can have a significant impact on quality of life. Women have reported negative effects on sexual health.[36] Women with BV report feeling self-conscious and uncomfortable and avoiding sexual encounters due to worries related to their symptoms.[36] The diligent NP can help improve quality of life and decrease clinic visits and costs for patients by focusing on improving outcomes for women with recurrent BV. More research studies are needed for increased treatment options for recurrent BV.

Microscopy provides enough diagnostic information in most cases. Newer technology such as DNA-probe or PCR-based testing may be required for more challenging clinical scenarios where an accurate diagnosis is hard to attain.

Conclusion

Large numbers of women are affected by BV. Providers should be well informed about BV as it is very likely that the condition will be encountered in clinical practice due to its high prevalence. It is essential that providers remain current on the latest therapies and research as current treatment regimens do not eliminate the disease in the majority of women. BV in women increases the risk of HIV, therefore, prevention and treatment can aid in reducing the spread of HIV and other sexually transmitted diseases. NP

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Recurrent bacterial vaginosis

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